PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 57666WO003	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US 03/08710	International filing date *(day/month/year)* 21.03.2003	Priority date *(day/month/year)* 05.04.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/12		
Applicant 3M INNOVATIVE PROPERTIES COMPANY et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.10.2003	09.07.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Luangkhot, N Telephone No. +49 89 2399-7857

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US 03/08710

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-25 as originally filed

Claims, Numbers

1-17 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-17
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-17
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1) The documents cited in the International Search Report (ISR) were numbered respectively from D1-D5; this numbering results from the citation order in the ISR and will be used for the procedure. Unless otherwise specified, the **cited passages of each document in the ISR will be considered.**

2) **Novelty and inventive step according to Art. 33(2) and 33(3) PCT**

2a) For the present examination it would be **assumed** that the priority date of present application is valid so that the P-documents D1-D2 which fall under the definition of Rule 70.10 PCT are not considered for the PCT phase. However the applicant's attention is drawn with the fact that Documents D1-D2 will be relevant for the European Regional Phase with regard to novelty **and eventually** inventive step.

2b) Claim 1 and its dependent claims 2-17 are novel **over D3-D5** because none of the cited documents describe an aerosol formulation comprising formoterol (Fo), mometasone (Mo), a propellant (HFA) and a bulking agent (BA) **wherein** the BA has a mass median diameter of **less than one micron.**

2b) The subject-matter of present application seems to lack the necessary inventive step for the following reasons:

D4 (see examples 25-33 and claim 10), filed by the same applicant, is directed to a pMDI formulation containing formoterol, a propellant, ethanol and eventually a surfactant.
The difference with present application resides in the fact that the formulation of D4 does not contain mometasone.
The problem to be solved can be seen as providing a formulation for MDI containing formoterol **and mometasone.**

As combination of drugs is a **frequent and common practice** in the field of "drug-delivery to the lungs for the treatment of respiratory disorders" (in particularly combination of a beta-agonist with a glucocorticoid) and there is no indication in prior art stipulating that the combination of formoterol with mometasone is not feasible (a combination of formoterol and mometasone is already described in D3

for examples and the cited patent literature in present application), the skilled man in the art does not need to be inventive by adding mometasone to the formulation of D4 and thus arrives at the claimed composition of present application with the obtention of the same advantages as described in D4 (slow flocculation, better content uniformity).
As long as applicant does not **providence evidence of a surprising effect,** the claimed composition would be considered as an **obvious** combination that the skilled man in the art wil perform routinely.

Therefore in view of the disclosure D4 claims 1-17 do not involve an inventive step.

2c) D3, document cited in present application, is directed to a suspension formulation for MDI containing formoterol, mometasone, a propellant and eventually ethanol (see p.3 last §- p.4 1st§). The difference with present application consists in that the formulation of D3 does not contain a **bulking agent (BA).**
The effect attributed to the use of a BA is a better content uniformity because the suspension is better stabilized or sets slower. This effect is demonstrated by applicant comparing bulked and non-bulked formulation.
The problem can be seen as providing a formulation permitting an improved content uniformity.
D4 (see p.5 L.1-30, examples 16-22,25-33) teaches that the use of a **BA** in a pMDI formulation (containing formoterol, a propellant, ethanol and optionally a surfactant) permits the drug to flocculate slowlier thus improving the dosing characteristics.

The skilled man in the art, willing to provide a formulation with an improved content uniformity, will use the teaching of D4 for the formulation of D3, and thus arrives at the claimed composition of present application with the obtention of the same advantages as described in D4.

As long as applicant does not **providence evidence of a surprising effect,** the claimed composition would be considered as an **obvious** combination that the skilled man in the art wil perform routinely.

Therefore in view of the D3 combined with D4 claims 1-17 do not involve an inventive step.

2d) This could be argued that the core of present application resides in the fact that the **size of the BA is smaller than 1 micron**, which is a feature that is not mentioned in D4. However D4 shows in the examples that flocculation is delayed (thus permitting reproducible dosing) thanks to the use of a BA, **no matter** the size of the BA.
As long as applicant does not show with support of experimantal tests comparing **microsized versus nanosized BA,** the size of the BA can not be acknowledged as an **essential feature which could confer inventiveness to the said subject-matter**. Therefore this feature will be seen as an obvious alternative which is not **mandatory**.

2e) Any information the applicant may wish to submit concerning the subject-matter of the invention, for example further details of its advantages or of the problem it solves, and for which there is no basis in the application as filed, should be confined to the letter of reply **and not** be incorporated into the application.

3) Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D4 is not mentioned in the description, nor are these documents identified therein.